Fixed-Dose Clindamycin Phosphate 1.2%, Benzoyl Peroxide 3.1%, and Adapalene 0.15% Gel for Moderate-to-Severe Acne: Phase 2 Study of the First Triple-Combination Drug

James Q Del Rosso, DO[1-3]; Leon H Kircik, MD[4-6]; Linda Stein Gold, MD[7]; Hilary Baldwin, MD[8,9]; Jonathan S Weiss, MD[10,11]; David M Pariser, MD[12,13]; Valerie Callender, MD[14,15]; Edward Lain, MD, MBA[16]; Michael Gold, MD[17]; Kenneth Beer, MD[18]; Zoe D Draelos, MD[19]; Neil Sadick, MD[20,21]; Radhakrishnan Pillai, PhD[22]; Varsha Bhatt, PhD[22]; Emil A Tanghetti, MD[23]

[1]JDR Dermatology Research/Thomas Dermatology, Las Vegas, NV; [2]Advanced Dermatology and Cutaneous Surgery, Maitland, FL; [3]Touro University Nevada, Henderson, NV; [4]Indiana University School of Medicine, Indianapolis, IN; [5]Physicians Skin Care, PLLC, Louisville, KY; [6]Icahn School of Medicine at Mount Sinai, New York, NY; [7]Henry Ford Hospital, Detroit, MI; [8]The Acne Treatment and Research Center, Brooklyn, NY; [9]Robert Wood Johnson University Hospital, New Brunswick, NJ; [10]Georgia Dermatology Partners, Snellville, GA; [11]Gwinnett Clinical Research Center, Inc., Snellville, GA; [12]Eastern Virginia Medical School, Norfolk, VA; [13]Virginia Clinical Research, Inc., Norfolk, VA; [14]Callender Dermatology and Cosmetic Center, Glenn Dale, MD; [15]Howard University College of Medicine, Washington DC; [16]Austin Institute for Clinical Research, Austin, TX; [17]Tennessee Clinical Research Center, Nashville, TN; [18]University of Miami Miller School of Medicine, Miami, FL; [19]Dermatology Consulting Services, PLLC, High Point, NC; [20]Weill Cornell Medical College, New York, NY; [21]Sadick Dermatology, New York, NY; [22]Bausch Health US, LLC, Petaluma, CA*; [23]Center for Dermatology and Laser Surgery, Sacramento, CA

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SYNOPSIS

- The pathogenesis of acne is multifactorial, involving follicular proliferation of *Cutibacterium acnes*, increased sebum production and inflammation, and abnormal keratinization[1,2]
  - Effective treatment requires pharmacologic targeting of one or more of these pathophysiologic mechanisms[2]
- There are numerous prescription oral and topical treatments for acne such as benzoyl peroxide (BPO), retinoids, antibiotics, and hormonal therapies[2]
- Combining three acne treatments (an antibiotic, antibacterial, and retinoid) in a once-daily topical polymeric dispersion formulation may provide greater efficacy and tolerability than single or dyad treatments
- This is the first study of clindamycin phosphate 1.2%/BPO 3.1%/adapalene 0.15% (IDP-126) gel, which once approved will be the first triple-combination, fixed-dose topical acne treatment

OBJECTIVE

- To evaluate the efficacy, safety, and tolerability of IDP-126 in participants with moderate-to-severe acne

METHODS

- In a phase 2, double-blind, multicenter 12-week study (NCT03170388),[3] participants aged ≥9 years with moderate-to-severe acne were randomized (1:1:1:1:1) to once-daily IDP-126 gel, vehicle gel, or 1 of 3 component dyad combination gels
- The Evaluator's Global Severity Score (EGSS) was scored as follows: 0 (clear) = Normal, clear skin/no evidence of acne; 1 (almost clear) = Rare noninflammatory lesions, with rare noninflamed papules; 2 (mild) = Some noninflammatory lesions, with few inflammatory lesions; 3 (moderate) = Noninflammatory lesions predominate, with multiple inflammatory lesions: several/many comedones and papules/pustules, ≤1 nodulocystic lesion; 4 (severe) = Inflammatory lesions more apparent, many comedones/papules/pustules, ≤2 nodulocystic lesions
- CeraVe® hydrating cleanser and CeraVe® moisturizing lotion (L'Oreal, NY) were provided as needed for optimal moisturization/cleaning of the skin
- Endpoints were treatment success at week 12 (≥2-grade reduction from baseline in EGSS and clear/almost clear skin) and least-squares (LS) mean changes from baseline to week 12 in inflammatory/noninflammatory lesions
- Treatment-emergent adverse events (TEAEs) and cutaneous safety and tolerability (via 4-point scale where 0=none and 3=severe) were also assessed

RESULTS

Participants

- A total of 741 participants were enrolled (intent-to-treat population: n=740; safety population: n=725)
- Mean age was approximately 19.5 years, most participants were female and White, and most had moderate disease (EGSS 3) at baseline (**Table 1**)
- Treatment compliance across treatment groups was ≥93%

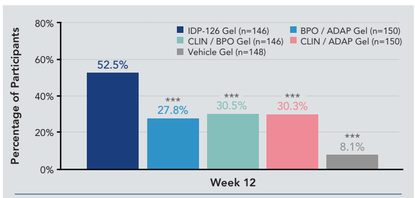
Efficacy

- At week 12, over half of participants achieved treatment success with IDP-126 vs ~30% or less with vehicle and dyads ($P \leq 0.001$, all; **Figure 1**)
- IDP-126 also demonstrated significantly greater absolute reductions in the number of inflammatory and noninflammatory lesions vs vehicle or dyads, ($P<0.05$, all) corresponding to >70% reductions (**Figure 2**)
- Images depicting acne improvements in IDP-126-treated participants are shown in **Figure 3**

Safety

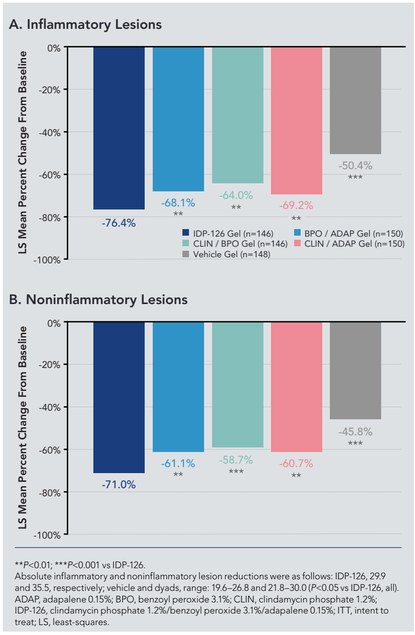
- TEAE rates were higher with IDP-126 and BPO/adapalene vs clindamycin/BPO, clindamycin/adapalene, or vehicle at week 12 (**Table 2**)
- Most TEAEs were of mild-to-moderate severity (data not shown)
- With IDP-126, there was no severe scaling, erythema, hypopigmentation, or itching, and <5% of participants had severe hyperpigmentation, burning, or stinging (**Table 3**)

FIGURE 1. Treatment Success[a] at Week 12 (ITT Population)



***$P<0.001$ vs IDP-126.
[a]Defined as at least a 2-grade reduction from baseline in Evaluator's Global Severity Score and a score of 0 (clear) or 1 (almost clear).
ADAP, adapalene 0.15%; BPO, benzoyl peroxide 3.1%; CLIN, clindamycin phosphate 1.2%; IDP-126, clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15%; ITT, intent to treat.

FIGURE 2. Lesion Reductions at Week 12 (ITT Population)



**$P<0.01$, ***$P<0.001$ vs IDP-126.
Absolute inflammatory and noninflammatory lesion reductions were as follows: IDP-126, 29.9 and 35.5, respectively; vehicle and dyads, range: 19.6–26.8 and 21.8–30.0 ($P<0.05$ vs IDP-126, all).
ADAP, adapalene 0.15%; BPO, benzoyl peroxide 3.1%; CLIN, clindamycin phosphate 1.2%; IDP-126, clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15%; ITT, intent to treat; LS, least-squares.

TABLE 1. Baseline Demographics and Characteristics (ITT Population)

	IDP-126 Gel (n=146)	BPO / ADAP Gel (n=150)	CLIN / BPO Gel (n=146)	CLIN / ADAP Gel (n=150)	Vehicle Gel (n=148)
Age, mean (SD), y	19.9 (7.0)	19.2 (8.0)	19.6 (6.9)	19.4 (6.5)	19.6 (7.1)
Female, n (%)	94 (64.4)	86 (57.3)	91 (62.3)	93 (62.0)	89 (60.1)
Race,[a] n (%)					
White	98 (67.1)	109 (72.7)	101 (69.2)	109 (72.7)	95 (64.2)
Black	24 (16.4)	26 (17.3)	30 (20.5)	20 (13.3)	26 (17.6)
Asian	10 (6.8)	6 (4.0)	8 (5.5)	9 (6.0)	17 (11.5)
Inflammatory lesion count, mean (SD)	39.0 (11.8)	39.0 (10.2)	40.0 (12.8)	38.2 (7.9)	38.2 (9.2)
Noninflammatory lesion count, mean (SD)	51.8 (20.3)	48.0 (14.7)	49.2 (17.6)	51.1 (18.4)	50.7 (18.7)
EGSS, n (%)					
3 – Moderate	124 (84.9)	119 (79.3)	124 (84.9)	129 (86.0)	127 (85.8)
4 – Severe	22 (15.1)	31 (20.7)	22 (15.1)	21 (14.0)	21 (14.2)

[a]Additional races not shown: American Indian/Alaska Native, Native Hawaiian/Other Pacific Islander, and Other/Multiple.
ADAP, adapalene 0.15%; BPO, benzoyl peroxide 3.1%; CLIN, clindamycin phosphate 1.2%; EGSS, Evaluator's Global Severity Score; IDP-126, clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15%; ITT, intent to treat; SD, standard deviation.

TABLE 2. Summary of Adverse Events (Safety Population)

Participants, n (%)	IDP-126 Gel (n=141)	BPO / ADAP Gel (n=146)	CLIN / BPO Gel (n=144)	CLIN / ADAP Gel (n=148)	Vehicle Gel (n=146)
Reporting any TEAE	51 (36.2)	52 (35.6)	26 (18.1)	40 (27.0)	22 (15.1)
Reporting any SAE[a]	1 (0.7)	0	0	3 (2.0)	0
Discontinued due to TEAE[b]	4 (2.8)	8 (5.5)	0	3 (2.0)	2 (1.4)
Related TEAEs	28 (19.9)	32 (21.9)	3 (2.1)	18 (12.2)	2 (1.4)
Related TEAEs (in ≥5% of participants in any treatment group)					
AS pain	11 (7.8)	16 (11.0)	1 (0.7)	5 (3.4)	1 (0.7)
AS dryness	9 (6.4)	8 (5.5)	2 (1.4)	9 (6.1)	0
TEAEs leading to discontinuation[c] (in ≥2% of participants in any treatment group)					
AS pain	2 (1.4)	5 (3.4)	0	2 (1.4)	0

[a]None of the SAEs were considered related to study drug.
[b]1 participant in the vehicle gel group discontinued the study drug, but not the study, due to a TEAE.
[c]Permanent withdrawal of study drug and/or early study discontinuation.
ADAP, adapalene 0.15%; AE, adverse event; AS, application site; BPO, benzoyl peroxide 3.1%; CLIN, clindamycin phosphate 1.2%; IDP-126, clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15%; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

TABLE 3. Severe (Grade 3) Cutaneous Safety and Tolerability Assessments[a] (Safety Population)

Participants, n (%)	IDP-126 Gel (n=141)	BPO / ADAP Gel (n=146)	CLIN / BPO Gel (n=144)	CLIN / ADAP Gel (n=148)	Vehicle Gel (n=146)
Scaling	0	2 (1.4)	0	2 (1.4)	0
Erythema	0	2 (1.4)	0	3 (2.0)	0
Hyperpigmentation	2 (1.4)	3 (2.1)	2 (1.4)	3 (2.0)	1 (0.7)
Itching	0	1 (0.7)	0	0	1 (0.7)
Burning	6 (4.3)	8 (5.5)	0	1 (0.7)	0
Stinging	3 (2.1)	6 (4.1)	0	0	0

[a]Investigator-assessed evaluations were scaling, erythema, hypopigmentation, and hyperpigmentation; participant-assessed evaluations were itching, burning, and stinging. Hypopigmentation is not shown as there were no severe cases.
ADAP, adapalene 0.15%; BPO, benzoyl peroxide 3.1%; CLIN, clindamycin phosphate 1.2%; IDP-126, clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15%.

FIGURE 3. Acne Improvements with IDP-126

Individual results may vary. All participants self-reported ethnicity as Non-Hispanic/Latino.
EGSS, Evaluator's Global Severity Score; IDP-126, clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15%; IL, inflammatory lesions; NIL, noninflammatory lesions.

CONCLUSIONS

- Once-daily treatment with the novel fixed-dose triple-combination clindamycin phosphate 1.2%/BPO 3.1%/adapalene 0.15% gel (IDP-126) in a polymeric dispersion system showed superior efficacy to vehicle gel and three dyad component gels over 12 weeks in this phase 2 study of adult, adolescent, and pediatric participants with moderate-to-severe acne
- IDP-126 was also safe and well tolerated with low rates of discontinuations
- Overall, the efficacy and safety profiles of IDP-126 demonstrate its potential as a new treatment option in the acne armamentarium

REFERENCES

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AUTHOR DISCLOSURES

JQDR has served as a consultant, investigator, and/or speaker for Ortho Dermatologics, Abbvie, Amgen, Arcutis, Dermavant, EPI Heath, Galderma, Incyte, LEO Pharma, Lilly, MC2 Therapeutics, Pfizer, Sun Pharma, and UCB LHK has acted as an investigator, advisor, speaker, and consultant for Ortho Dermatologics. LSG has served as investigator/consultant or speaker for Ortho Dermatologics, LEO Pharma, Dermavant, Incyte, Novartis, AbbVie, Pfizer, Sun Pharma, UCB, Arcutis and Lilly. HB has served as advisor, investigator, and on speakers' bureaus for Almirall, Cassiopea, Foamix, Galderma, Ortho Dermatologics, Sol Gel, and Sun Pharma. JSW is a consultant, speaker, advisor, and/or researcher for AbbVie, Ortho Dermatologics, Janssen Biotech, Dermira, Almirall, Brickell Biotech, DermTech, Scynexis. DMP has served as consultant to Atacama Therapeutics, Bickel Biotechnology, Biofrontera AG, Celgene, Dermira, LEO Pharma, Regeneron, Sanofi, TDM SurgiTech, TheraVida, and Ortho Dermatologics; investigator for Abbott Laboratories, Almirall, Amgen, ACBiome, Asana Biosciences, Bickel Biotechnology, Celgene, Dermavant, Dermira, Eli Lilly, LEO Pharma, Menlo Therapeutics, Merck & Co., Novartis, Novo Nordisk A/S, Ortho Dermatologics, Pfizer, Regeneron, and Stiefel; on advisory board for Pfizer; and on the data monitoring board for BMS. VC has served as an investigator, consultant, or speaker for AbbVie, Galderma, L'Oréal, Ortho Dermatologics, and Vyne. EL has nothing to disclose. MG has acted as an investigator, advisor, speaker, and consultant for Ortho Dermatologics. KB has received funding from Allergan, Galderma, Evolus, and Revance. ZDD received research funding from Ortho Dermatologics. NS has served on advisory boards, as a consultant, investigator, speaker, and/or other and has received honoraria and/or grants/research funding from Almirall, Actavis, Allergan, Anacor Pharmaceuticals, Auxilium Pharmaceuticals, Bausch Health, Bayer, Biorasi, BTG, Carma Laboratories, Cassiopea, Celgene Corporation, Cutera, Cynosure, DUSA Pharmaceuticals, Eclipse Medical, Eli Lilly and Company, Endo International, EndyMed Medical, Ferndale Laboratories, Galderma, Gerson Lehrman Group, Hydropeptide, Merz Aesthetics, Neostrata, Novartis, Nutraceutical Wellness, Palomar Medical Technologies, Prescriber's Choice, Regeneron, Roche Laboratories, Samumed, Sciton Medical, Stora Medical AG, Sunera Medical, Vanda Pharmaceuticals, and Venus Concept. VB and RP are employees of Bausch Health US, LLC and may hold stock and/or stock options in its parent company. EAT has served as speaker for Novartis, Ortho Dermatologics, Sun Pharma, Lilly, Galderma, AbbVie, and Dermira; served as a consultant/clinical studies for Hologic, Ortho Dermatologics, and Galderma; and is a stockholder for Accure..

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